

Docket No.: PHOE0001-100  
Filing Date: September 29, 2003

PATENT  
Serial No.: 10/674,666

# AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Please rewrite paragraph [00055] as follows:

[00055] As used herein, the term "selectively inhibit" refers selective inhibition of viral replication and is, in some embodiments, the ratio of  $CC_{50}/EC_{50}$   $IC_{50}$  of viral mRNA levels. An  $SI > 10$  is considered to reflect a selective inhibition of viral replication.

Please rewrite paragraph [00157] as follows:

[00157] Dividing cultures of AVA5 cells were treated with various concentrations of PEG-ADI (or in control experiments alpha interferon or ribavirin) for 3 days. HCV mRNA levels were assayed as above. Cell viability was determined using neutral red. The concentrations which inhibit 50% ( $IC_{50}$ ) and 90% ( $IC_{90}$ ) of HCV mRNA levels were determined. The concentration of drug which kills 50% of the cells ( $CC_{50}$ ) was also determined. The  $CC_{50}/EC_{50}$   $IC_{50}$  is calculated to determine the selectivity index (SI). An  $SI > 10$  is considered to be a selective inhibition of the viral replication. The results are shown below.

Drug	$CC_{50}$	$IC_{50}$	$IC_{90}$	SI
ADI-PEG20	0.335 IU/ml	<del>0.27</del> 0.027 IU/ml	0.188 IU/ml	12
alpha interferon	>10000 IU/ml	2.1 IU/ml	9.0 IU/ml	>4762
ribavirin	74 $\mu$ M	>10 $\mu$ M	>10 $\mu$ M	NA

These data confirm that ADI-PEG20 inhibits HCV replication and that this drug is selective.